

## REMARKS

### I. The Subject Matter of the Claims

The subject matter of the claims relates generally to methods of generating specific nucleic acids of greater length than a typical SAGE tag, providing a material that is amenable to further characterization and thereby facilitating resolution of multiple SAGE tag identifications and assignment of orphan SAGE tags to genes.

### II. The Amendments

The specification has been amended to insert sequence identifiers (i.e., SEQ ID NOs) in accordance with 37 C.F.R. §§ 1.821-1.825. In addition, a substitute sequence listing is being filed herewith. The specification has also been amended to remove citations to websites. The claims generally have been amended to address 35 U.S.C. §112, second paragraph, matters of form and clarity. The amended claims clarify the nature of the claimed subject matter without narrowing the scope thereof. In some instances, the scope of a claim has been broadened to more accurately reflect the true scope of the invention.

Claim 5 has been amended to properly depend from claim 3.

### III. Traversal of Restriction requirement

In response to the restriction requirement set forth in the Office Action, Applicants herein confirm election of group I, claims 1 through 20, for continued prosecution in the application, with traverse.

Applicants request that the restriction requirement be reconsidered because the Examiner has not shown that a serious burden would be required to examine all of the claims. M.P.E.P. § 803 provides:

If the search and examination of an application can be made without serious burden, the Examiner **must** examine it on the merits, even though it includes claims to distinct or independent inventions. (*Emphasis added.*)

Thus, for a restriction to be proper, the Examiner must satisfy the following two criteria: (1) that independent and distinct inventions are being claimed (35 U.S.C. § 121); and (2) that the search and examination of the entire application cannot be made without serious burden. See M.P.E.P. § 803.

Applicants respectfully submit that the Examiner has not shown that these criteria have been satisfied. Specifically, the Examiner has not shown that it would be a serious burden to search and examine groups I-III together. A search relating to the methods of identifying genes of Group II would significantly overlap with the methods for characterizing a SAGE tag fragment of Groups I and III, and very similar, if not identical, searches would be performed for the methods of Groups I and III. Accordingly, the Examiner has not shown that an undue burden would be produced by the combined search. Thus, Applicants submit that the restriction requirement has been overcome and all claims may properly be considered in the present application.

#### **IV. Patentability Arguments**

##### **A. The Rejection of Claims 1-20 under 35 U.S.C. §112, Second Paragraph, Should Be Withdrawn**

Claims 1-20 were rejected by the Examiner for assertedly failing to point out and distinctly claim the subject matter which Applicants regard as the invention because it is unclear what is meant by the phrase "cDNA fragments that correspond to the SAGE tag." In response, the Applicants have amended claim 1 to clarify the subject matter without narrowing the scope of the claimed subject matter. As such, this basis for rejecting claims 1-20 under 35 U.S.C. §112, second paragraph, has been overcome.

Claim 5 was rejected by the Examiner as assertedly being vague and indefinite because of the phrase "the  $Mg^{2+}$  concentration is 4 mM." In response, the Applicants have amended claim 5 to clarify the claimed subject matter and overcome the asserted antecedent basis rejection without narrowing the scope of the claim. Accordingly, the assertion that there is no antecedent basis is moot and Applicants submit that this basis for rejecting claim 5 under 35 U.S.C. §112, second paragraph, has been overcome.

Claim 7 was rejected by the Examiner as assertedly being vague and indefinite because of the phrase "said base excluding dT." The Applicants have amended claim 7 to clarify the nature of the claimed subject matter. Specifically, the phrase "single base anchored primer" has been substituted for the phrase "single-base anchored oligo-dT primer" to more clearly define the claimed subject matter. Claim 7, as amended, depends from claim 1 and further recites that the single base (other than dT) is anchored to the 3' end of the string of dT nucleotides. Additionally, the Applicants have added the term "single" with respect to the base

excluding dT to indicate that the single base at the 3' end of the primer is any base other than dT. The Applicants cite to the specification as originally filed at page 9, line 26, wherein it states that "[t]he single base may be dA, dG, or dC." The Applicants additionally note that claim 1 has been amended herein to substitute a "single base anchored primer" for "single-base anchored oligo-dT primer," in conformity with amended claim 7. Accordingly, the Applicants submit that the present amendment and disclosure in the specification obviates the instant basis for rejecting claim 7 under 35 U.S.C. §112, second paragraph.

The Examiner rejected claim 13 for assertedly being vague and indefinite because the phrase "sequence in existing DNA databases" is unclear in identifying what sequence can be found in the existing databases. In response, the Applicants have amended claim 13 to substitute the term "known," as recited in original claim 14, for the reference to existing DNA databases. Accordingly, it would be apparent to one of ordinary skill in the art that "known" sequences are those sequences that can be found in the public domain, such as in public databases. The specification as originally filed (see, e.g., page 34, lines 15-20) states that "[t]he sequences generated using GLGI can be used to match gene databases (e.g., GenBank, EMBL, DDBJ, UniGene Human Database)." Thus, it would be apparent to one of ordinary skill in the art that analyzing a cDNA sequence according to claim 13 would involve comparing the cDNA sequence to known sequences such as those sequences found in existing databases, as taught in the specification. As such, this basis for rejecting claim 13 under 35 U.S.C. §112, second paragraph, has been overcome.

Claims 15 and 20 were rejected for assertedly being vague and indefinite because the phrase "the full-length cDNA" lacks antecedent basis. The Applicants have amended claim 15 to remove the term "the" and replaced it with the term "a", addressing a formal matter without narrowing the scope of the claim. This amendment to claim 15 renders moot the instant basis for rejecting claim 15 and for rejecting claim 20, which is dependent on claim 15.

For the foregoing reasons, the Applicants submit that the rejection of claims 1-20 under 35 U.S.C. § 112, second paragraph, has been overcome and should be withdrawn.

**B. The Rejection of Claims 1-3, 5-9, 11-12, and 15 under 35 U.S.C. §103(a) Should Be Withdrawn**

The Examiner rejected various claims under 35 U.S.C. § 103(a) over van den Berg *et al.* in view of various secondary references. More particularly, claims 1-3, 5-9, 11-12,

and 15 were rejected under § 103(a) over van den Berg *et al.* in view of Liang *et al.* Claim 4 was rejected under § 103(a) over van den Berg *et al.* in view of Liang *et al.* and Lundberg *et al.* Claim 10 was rejected under § 103(a) over van den Berg *et al.* in view of Liang *et al.* and Spinella. Finally, claims 13, 14, 18 and 20 were rejected under § 103(a) over van den Berg *et al.* in view of Liang *et al.* and Velculescu *et al.*

In support of the rejection, the Examiner relied on van den Berg *et al.* for the disclosure of a method of serial analysis of gene expression that utilizes a tag-specific primer and an antisense primer such as a poly(dT) primer. The Examiner further points out that van den Berg *et al.* discloses that the products of such methods may be used to identify gene-specific sequence information, to isolate full-length cDNA clones, and to analyze tissue-specific gene expression. The Examiner also points out that van den Berg *et al.* discloses optimization of PCR conditions, including MgCl<sub>2</sub> concentration.

With respect to the secondary references, the Examiner relied on Liang *et al.* as disclosing a method of identifying and analyzing altered gene expression at the mRNA level in any eukaryotic cell in which one single-base-anchored oligo (dT) primer is used. Lundberg *et al.* assertedly discloses the use of Pfu DNA polymerase for PCR. Spinella assertedly discloses a method of obtaining short DNA tags involving a 5' adaptor containing a restriction endonuclease recognition site (*Bam*HI). Velculescu *et al.* assertedly discloses a method of using SAGE tags to characterize a large number of transcripts, involving the generation and cloning of ditags and quantitative characterization of SAGE tag-based analyses.

In response, the Applicants traverse the rejection. The van den Berg *et al.* reference was apparently accepted for publication on July 19, 1999 and was published in September, 1999. The instant application claims the priority benefit of provisional U.S. Patent Application No. 60/173,617, which was filed on December 29, 1999. Accordingly, van den Berg *et al.* is apparently available as a reference under 35 U.S.C. § 102(a).

Attached hereto as Appendix A is the Declaration of San Ming Wang, Ph.D., Under 37 C.F.R. § 1.131. Dr. Wang is one of the named inventors of the instant application and, in the declaration, Dr. Wang asserts that the invention of the pending claims was completed prior in time to July 19, 1999, and, thus, prior to the September, 1999 publication date of van den Berg *et al.* To corroborate that assertion, relevant pages of Dr. Wang's laboratory notebook are attached as Exhibit A to that declaration. The Wang declaration establishes that the named

inventors of the instant application had completed the claimed invention prior in time to the publication of van den Berg *et al.* Accordingly, the attached declaration effectively removes van den Berg *et al.* as a reference available against any claims pending in the instant application.

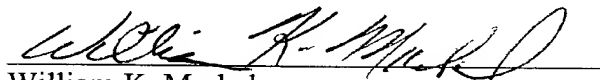
With van den Berg *et al.* unavailable as a reference against the pending claims, the Applicants submit that a *prima facie* case of obviousness cannot be maintained against any of the pending claims. More particularly, there is no support for the assertion that any of the following features were known in the art: a method of serial analysis of gene expression that utilizes a tag-specific primer and a poly(dT) primer; that the products of such methods may be used to identify gene-specific sequence information, to isolate full-length cDNA clones, and to analyze tissue-specific gene expression; or the optimization of PCR conditions, including MgCl<sub>2</sub> concentration. None of the cited secondary references (Liang *et al.*, Lundberg *et al.*, Spinella, Velculescu *et al.*) discloses any of these features, and the Examiner has not asserted that they do. Accordingly, the Applicants submit that a *prima facie* case of obviousness for any one of claims 1-3, 5-9, 11-12 and 15 under 35 U.S.C. § 103(a) over any combination of the cited references has not been established; accordingly, the rejection should be withdrawn.

#### CONCLUSION

In view of the amendments and remarks made herein, the Applicants submit that claims 1-20 are in condition for allowance and request notification of the same.

Respectfully submitted,  
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## **APPENDIX A**